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Anna Summers

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Ajay Hasmukhlal UPADHYAY
Serial No.:	09/879,320
Filing Date:	June 12, 2001
Docket No.:	RD 01022
Examiner:	Lakshimi S. Channavajjala
Art Unit:	1615
For:	COMPRESSIBLE GUAIFENESIN COMPOSITIONS, METHOD FOR MAKING SAME AND METHOD FOR MAKING COMPRESSED GUAIFENESIN DOSAGE FORMS THEREFROM

TRANSMITTAL LETTER

COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

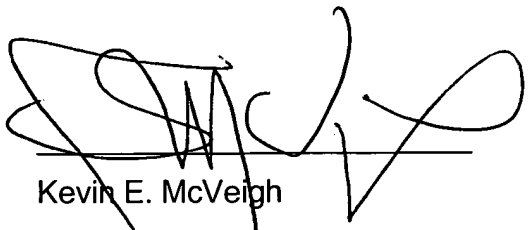
Transmitted herewith is the *Appeal Brief* in the above-referenced application, with respect to the *Notice of Appeal* filed on January 9, 2006.

Appellant requests under the provisions of 37 CFR 1.136 (a) to extend the period for filing the *Appeal Brief* for three (3) months, that is from February 9, 2006, to June 9, 2006.

The Director is hereby authorized to charge the fee of $500.00, due under 37 CFR 41.20 (b)(2), for this *Appeal Brief* and the fee of $1,020.00, due under 37

CFR 1.17 (a)(3) for the extension of time, as well as any other fees which may be required, or to credit any overpayment to Appellant's deposit account 181169.

Respectfully Submitted,



Kevin E. McVeigh
Reg. No. 33,017

Rhodia Inc.
8 Cedar Brook Drive
Cranbury, NJ 08512
(609) 860-4194
June 9, 2006

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APPEAL BRIEF

Commissioner of Patents
P.O. Box l450
Alexandria, VA 22313-l450

This *Appeal Brief* is in response to the *Final Rejection* dated 10/19/2005.

(i) Real Party in Interest

The real party in interest is Rhodia Inc., a Delaware corporation having its principle place of business at 8 Cedar Brook Drive, Cranbury, NJ 08512.

(ii) Related Appeals and Interferences

There are no prior or pending appeals, interferences, or judicial proceedings known to appellant, appellant's legal representative, or assignee that is related to or that may directly affect, be directly affected by, or have a bearing on the board's decision in this appeal.

(iii) Status of Claims

Claims 5, 9-30, and 32 have been canceled.

Claims 1-4, 6-8, 31, and 33-36 are pending.

Claims 1-4, 6-8, 31, and 33-36 stand finally rejected.

The final rejection of Claims 1-4, 6-8, 31, and 33-36 is appealed.

Claims 1-4 and 6-8 stand or fall together. Claims 31 and 33-36 stand or fall together and are separately patentable over claims 1-4 and 6-8 for the reasons discussed below.

(iv) Status of Amendments

No amendments have been filed subsequent to the final rejection.

(v) Summary of Claimed Subject Matter

Appellant's Claim 1 is directed to a particulate guaifenesin composition that:

- contains from about 85 percent by weight to about 97.5 percent by weight guaifenesin (guaifenesin is pharmaceutical active ingredient used, for example, in cold medications),
- contains particles that comprise an agglomerated mixture of guaifenesin particles and a polyvinylpyrrolidone binder, and
- wherein less than about 30 percent by weight of the particles of the composition exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers, as determined by sieve analysis, based on the total weight of the composition.

Appellant's Claim 31 is directed to a guaifenesin composition that:

- contains from about 85 percent by weight to about 97.5 percent by weight guaifenesin particles, a polyvinylpyrrolidone binder, and a solubilizer, or a disintegrant, or a solubilizer and a disintegrant is capable of being compressed into a compressed dosage form without addition of other components,
- is in the form of particles, including particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrolidone binder, and
- wherein less than about 30 percent by weight of the particles of the composition exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers, as determined by sieve analysis, based on the total weight of the composition.

(vi) Grounds of Rejection to be Reviewed on Appeal

Claims 1-4, 6-8, 31, and 33-36 stand finally rejected under 35 USC §103(a) as being unpatentable over U.S. Patent No. 4,798,725 to Patel ("Patel").

The Examiner states that Patel teaches a pharmaceutical composition for oral administration that comprises a flowable particulate mixture of active drug (0.01% to 90%), polyvinylpyrrolidone (5% to 96%), and a carboxyvinyl polymer, wherein the particles have a size such that they pass through a 60 mesh.

The examiner states that 60 mesh is, according the instant specification 250 microns, and then asserts that the particles of Patel are thus within appellant's claimed ranges, i.e., < 30% of the articles have a size greater than 425 microns, and > 80% of the particles have a size greater than 45 microns. The examiner interprets the particle size limitations of appellant's claims to require only that the size of the instant particles is between 45 and 425 microns, and concludes that the claim limitations thus includes the 250 microns particles of Patel.

The examiner acknowledges that Patel does not teach the following claim limitations:

- agglomerated mixture,
- percentages of the amounts of guaifenesin,
- the particles of specific sizes, and
- specific solubilizer maltodextrin.

The examiner points out that Example 7 of Patel is directed to a composition of particulate mixture of guaifenesin together with PVP, talc, zinc stearate, and Carbopol. The examiner urges that Patel teaches a particulate mixture of the same active ingredient and binder as claimed and the particle sizes used by Patel are in the same range as claimed, that Patel suggests high amounts of active ingredient (as high as 90%), that addition of pharmaceutical excipients such as silicon dioxide, stearic acid, talc, and other conventional additives.

The examiner concludes that it would have been obvious for one of ordinary skill in the art at the time the invention was made to optimize the amounts of particulate guaifenesin, PVP and other additives, choose the particle sizes and the excipients in the composition of Patel

so as to achieve the desired flow rate of the particulate mixture of active and excipients and thus achieve a desired release pattern.

(vii) Argument

(a) Patel

Patel is directed to capsule for oral administration, comprising a capsule shell and the particulate mixture of Patel within the shell (see col. 2, lines 63-66 of Patel). The particulate mixture comprises a particles of an active drug ingredient, particles of polyvinylpyrrolidone, and particles of a carboxyvinylpolymer (see col. 3, lines 13-18 of Patel), is made by simply dry blending the particulate ingredients (col. 8, lines 13-17 of Patel), and is "flowable" (see col. 3, lines 1 - 13 of Patel). Guaifenesin is suitable as the active drug ingredient (see col. 6, line 32 and Col. 13, Example 7 of Patel).

(a) Agglomerated Mixture

Appellant submits that one of ordinary skill would not have found Appellant's claimed invention obvious in view of Patel because Patel does not disclose or suggest the limitations of Appellant's claim requiring particles of an agglomerated mixture of guaifenesin particles and polyvinylpyrrolidone.

Patel does not teach particles that comprise an agglomerated mixture of guaifenesin and polyvinylpyrrolidone, as required by Appellant's claims 1 and 31. (The particles of agglomerated mixture are generally formed by mixing a mixture comprising guaifenesin, polyvinylpyrrolidone, and water under high shear to form agglomerates, wet milling the agglomerates to reduce their size, drying the wet milled agglomerates, and classifying the dried particles of agglomerated mixture to control the particle size distribution of the particles (see p. 8, line 6 to p. 11, line 8 of the present application). In contrast, the particulate mixture of Patel is disclosed as a simple mixture made by dry blending of particulate ingredients (col. 8, lines 13-17 of Patel).

Appellant submits that Patel discloses use of polyvinylpyrrolidone as a sustained release agent and does not disclose, suggest, or provide any motivation for making particles that comprise an agglomerated mixture of guaifenesin and polyvinylpyrrolidone, as required by Appellant's claims 1 and 31. The polyvinylpyrrolidone component of Patel functions as a sustained release agent by providing for the formation of a cohesive mass of active ingredient, polyvinylpyrrolidone and gastric juices (see col. 3, lines 25 to 38 of Patel) upon being wetted by the gastric juices (col. 3, line 63 to col. 4, line 9 of Patel). Applicant acknowledges that the cohesive mass described by Patel could perhaps be characterized as an agglomerated mixture. However, Appellant submits that, by virtue of its cohesiveness, such mass cannot fairly be characterized as representing particles of an agglomerated mixture and that the cohesive mass, which apparently represents the entire contents of Patel's dosage form, would in any case fail to satisfy the particle size limitations of appellant's claims 1 and 31 (appellant's particle size limitations are discussed below).

The examiner has acknowledged that Patel does not teach agglomerated particles, but made no effort to remedy this deficiency. Appellant submits that the examiner's conclusion with respect to the obviousness of Appellant's claimed invention in view of Patel is fatally flawed in that it completely neglects Appellant's limitation requiring particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrrolidone. Appellant therefore submits that the examiner has failed to establish a case of *prima facie* obviousness of appellant's claims over Patel, because the examiner has failed to consider all the words of appellant's claims, see *In re Wilson,* 424 F.2d 1382, 165 U.S.P.Q. 494 (C.C.P.A. 1970).

(b) Particle Size and Flow Rate

Appellant submits that one of ordinary skill would not have found Appellant's claimed invention obvious in view of Patel because Patel does not disclose or suggest the

limitations of Appellant's claim requiring particles satisfying a specific particle size distribution.

As acknowledged by the examiner, Patel does not teach the exact percentages of the particles of specific sizes claimed by Appellant. However, the examiner states that Patel teaches that the particles have a size such that they pass through 60 mesh and are thus within Appellant's claimed particle size range. The examiner observes that according to claim 1 of the present application, < 30% of the particles have a size greater than 425 microns and >80% of the particles have a size greater than 45 microns and urges that the size of the instant particles is therefore between 45 and 425 microns, which includes 250 microns

Appellant submits that the particle size described by Patel refers only to the particle size of the polyvinylpyrrolidone component of the mixture of Patel (see col. 4, lines 17-20 of Patel), does not refer to the particle size of the particulate mixture of Patel, and, since the particulate mixture of Patel includes other particulate components in addition to polyvinylpyrrolidone particles, is not adequate to characterize the particle size distribution of the particulate mixture of Patel.

Appellant further submits that contrary to the examiner's assertions, Patel's teaching that the preferred polyvinlypyrrolidone particles have a size such that they pass through 60 mesh is not sufficient to establish that such particles are within the range of particle sizes claimed in Appellant's claims 1 and 31. Patel's expressed preference that the particle size of the polyvinylpyrrolidone component of Patel's mixture is such that 100 percent of the particles will pass through a 60 mesh sieve establishes only that the preferred polyvinylpyrrolidone particles are less than 250 micrometers in size, and does not disclose or in any way suggest that the preferred polyvinylpyrrolidone particles meet the limitation of Appellant's claims requiring that greater than about 80 percent by weight of the particles of the claimed composition exhibit a particle size of greater than 45 micrometers. For example, polyvinylpyrrolidone particles having a particle size distribution wherein 100 percent by weight of the particles have a particles size of 30

micrometers would satisfy Patel's preference for polyvinylpyrrolidone particles that pass through a 60 mesh screen, but would not satisfy the limitation of Appellant's claims requiring that greater than about 80 percent by weight of the particles of the claimed composition exhibit a particle size of greater than 45 micrometers.

Appellant submits that the examiner's conclusion with respect to the obviousness of Appellant's claimed invention in view of Patel is flawed in that the examiner has incorrectly interpreted and thereby failed to adequately consider appellant's limitation requiring greater than about 80 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers. Appellant therefore submits that the examiner has failed to establish a case of *prima facie* obviousness of appellant's claims over Patel, because the examiner has failed to consider all the words of appellant's claims, see *In re Wilson,* 424 F.2d 1382, 165 U.S.P.Q. 494 (C.C.P.A. 1970).

(c) Relative Amounts of Ingredients

Appellant submits that one of ordinary skill would not have found Appellant's claimed invention obvious in view of Patel because Patel effectively teaches away from the limitations of appellant's claims 31 and 33-36 requiring the specific combination of ingredients.

The examiner acknowledges that Patel does not disclose the claimed percentages of the amounts of guaifenesin, and specific solubilizer, maltodextrin, but broadly observes that Patel also suggests addition of the pharmaceutical excipients such as silicon dioxide, stearic acid, talc, and other conventional additives.

The composition of appellant's claims 31 and 33- 36 is a directly compressible composition that is capable of being compressed under relatively low compressive forces into a compressed dosage form that exhibits low friability and high hardness (see p. 29, lines 4-15 and the friability and hardness results for examples 110 in TABLES 2A-2E of the present application), without addition of other components. The solubilizer and/or

disintegrant components of the composition of appellant's claims 31-36 are included for the purpose of accelerating the disintegration (i.e., into particles) and dissolution of the compressed dosage form once the dosage form is administered to a patient (p. 6, lines 9-29 of the present application). In contrast, Patel is directed to capsule comprising a capsule shell and the particulate mixture of Patel within the shell. Patel teaches that the particulate mixture of Patel is to remain flowable (col. 8, lines 24-25 of Patel) and although capable of being lightly compressed into a "plug" of particulate material, such a plug is one that "can be easily broken under light pressure" and "is considered to be flowable herein" (col. 3, lines 1-13 of Patel) and that the particulate mixture of Patel is to remain as a particulate mixture within the capsule shell (see col. 8, lines 26-38 of Patel).

Appellant submits that, to the extent that Patel teaches the desirability of maintaining the flowability of Patel's particulate mixture and that the mixture remains flowable even after being compressed, Patel teaches away from modifying the components of the particulate mixture of Patel in a way that would result in directly compressible composition according to appellant's claims 31 and 33-36 or form adding excipients, such as solubilizers and/or disintegrants that would only be of use in a directly compressible composition.

Appellant therefore submits that the examiner has failed to establish a case of *prima facie* obviousness of appellant's claims 31 and 33-36 over Patel, because Patel teaches away from the invention set forth in those claims, see, e.g., *In re Hedges,* 783 F.2d 1038 228 U.S.P.Q. 685 (Fed. Cir. 1986).

Conclusion

For all of the reasons discussed above, appellant submits that the examiner has failed to establish a *prima facie* case that appellant's claimed invention is obvious in view of Patel and that the rejection of appellant's Claims 1-4, 6-8, 31, and 33-36 under 35 USC §103(a) as being unpatentable over Patel is therefore improper and should be overturned. Appellant now requests that the Appeal Board overturn that rejection.

(viii) Claims Appendix

1. A particulate guaifenesin composition, comprising particles that comprise an agglomerated mixture of guaifenesin particles and a polyvinylpyrrolidone binder, wherein the composition comprises from about 85 percent by weight to about 97.5 percent by weight guaifenesin and wherein by sieve analysis, based on the total weight of the composition, less than about 30 percent by weight of the particles of the composition exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers.

2. The composition of claim 1, wherein the composition comprises guaifenesin, polyvinylpyrrolidone binder, a solubilizer, a glidant, and a lubricant.

3. The composition of claim 1, wherein the composition comprises guaifenesin, polyvinylpyrrolidone binder, a maltodextrin, a silica, and stearic acid.

4. The composition of claim 1, wherein the composition, based on the total weight of dry ingredients, from about 85 to about 97.5 percent by weight guaifenesin, from about 1.0 to about 7 percent by weight polyvinylpyrrolidone binder, from about 0.2 to about 4 percent by weight of a solubilizer or a disintegrant or a solubilizer and a disintegrant, from about 0.1 to about 2 percent by weight of a glidant, and from about 0.1 to about 2 percent by weight of a lubricant.

6. The composition of claim 1, wherein by sieve analysis, based on the total weight of the guaifenesin particles, greater than about 10 percent by weight of the guaifenesin particles exhibit a particle size of greater than 75 micrometers and greater than about 55 percent by weight of the particles exhibit a particle size of greater than 45 micrometers.

7. The composition of claim 1, wherein less than about 25 percent by weight of the particles of the composition exhibit a particle size of greater than about 425 micrometers,

greater than about 85 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers, and from about 17 to about 55 percent by weight of the particles of the composition exhibit a particle size of from greater than 45 micrometers to less than 150 micrometers.

8. The composition of claim 1, wherein the composition exhibits a flow rate of greater than or equal to 6.5 grams per second, as measured using a VanKel flowmeter.

31. A guaifenesin composition, comprising guaifenesin particles, a polyvinylpyrrolidone binder, and a solubilizer, or a disintegrant, or a solubilizer and a disintegrant, wherein the composition comprises from about 85 percent by weight to about 97.5 percent by weight guaifenesin, and is in the form of particles, said particles of said composition comprising particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrolidone binder, wherein the composition is capable of being compressed into a compressed dosage form without addition of other components, and wherein by sieve analysis, based on the total weight of the composition, less than about 30 percent by weight of the particles exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles exhibit a particle size of greater than about 45 micrometers.

33. The composition of claim 31, wherein the composition comprises, based on the total weight of dry ingredients, from about 85 to about 97.5 percent by weight guaifenesin, from about 1.0 to about 7 percent by weight polyvinylpyrrolidone binder, and from about 0.2 to about 4 percent by weight of solubilizer, or disintegrant, or solubilizer and disintegrant.

34. The composition of claim 33, wherein the composition further comprises from about 0.1 to about 2 percent by weight of a glidant, and from about 0.1 to about 2 percent by weight of a lubricant.

35. The composition of claim 31, wherein less than about 25 percent by weight of the particles exhibit a particle size of greater than about 425 micrometers, greater than about 85 percent by weight of the particles exhibit a particle size of greater than about 45 micrometers, and from about 17 to about 55 percent by weight of the particles exhibit a particle size of from greater than 45 micrometers to less than 150 micrometers.

36. The composition of claim 31, wherein the composition exhibits a flow rate of greater than or equal to 6.5 grams per second, as measured using a VanKel flowmeter.

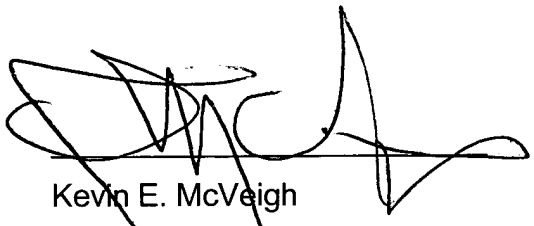
(xi) Evidence Appendix

No evidence has been entered into the record by the examiner.

(xii) Related Proceedings Appendix

There are no related proceedings.

Respectfully Submitted,



Kevin E. McVeigh
Reg. No. 33,017

Rhodia Inc.
8 Cedar Brook Drive
Cranbury, NJ 08512
(609) 860-4194
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